

The Amendment After Final filed on October 11, 2005, was fully responsive to the Final Office Action, but box no. 3 of the Advisory Action indicates that the Amendment was not entered. The accompanying RCE Transmittal requests entry of that earlier Amendment. The applicants also provide these Supplemental Remarks to address the issue raised by the Examiner in the personal interview regarding the treatment of seborrhea and seborrheic dermatitis.

All pending claims 14-23 and 26-29 recite treating seborrheic dermatitis by administering to a seborrheic dermatitis patient an amount effective for the treatment of seborrheic dermatitis of a composition comprising an active component that consists of the 1-hydroxy-2-pyridone of formula I, either in free form or as a pharmaceutically acceptable salt.

The Examiner rejected all claims as being anticipated by or as being obvious over U.S. Patent No. 5,650,145 to Saint-Leger ("Saint-Leger"). As explained in the Amendment After Final, the pending claims have been amended to recite "an active component consisting of" the claimed 1-hydroxy-2-pyridone. Saint-Leger, in contrast, teaches the use of two active components: an antifungal agent and antibacterial agent. Since the applicants' invention includes only one active component, the 1-hydroxy-2-pyridone, Saint-Leger cannot anticipate the claims.

Saint-Leger does not suggest the invention from an obviousness perspective either. The Examiner noted that Saint-Leger "describes a method for treating a male human patient with a composition applied to the scalp, resulting in a change in seborrhea." Final Office Action at page 4. Saint-Leger, however, teaches only reduction of and treatment of hair loss and some modification of seborrhea. Even though Saint-Leger mentions a variation in seborrhea in its Example 6, that does not equate with treatment of seborrheic dermatitis, and it furthermore does not suggest using the active component of the pending claims, on its own, in the treatment of seborrheic dermatitis.

The enclosed Declaration of James Leyden, M.D., supports the applicants' interpretation of the Saint-Leger disclosure. Paragraphs 5-6 of Dr. Leyden's Declaration contrast the conditions of seborrhea and seborrheic dermatitis. He explains that seborrhea is a condition of the sebaceous glands characterized by the excessive

production of sebum by the sebaceous glands which, when it reaches the skin surface, makes the skin appear oil or shiny and feel greasy. *Id.* at ¶ 5. Seborrhea does not involve the skin's keratinocytes, and does not cause seborrheic dermatitis. *Id.*

On the other hand, seborrheic dermatitis is not a condition of the sebaceous glands. *Id.* at ¶ 6 (citing Fitzpatrick's Dermatology in General Medicine, Vol. I, 6<sup>th</sup> ed., p. 1198 (attached as Exhibit B)). Rather, it is a chronic papulosquamous dermatosis, and a disorder characterized by the hyperproliferation of keratinocytes in the skin. *Id.* It is characterized by erythema (redness of the skin), scaling and yellow crusted patches. *Id.* Dr. Leyden explains that the sebaceous glands are not involved in seborrheic dermatitis, and excess sebum production is not a diagnostic feature of seborrheic dermatitis. *Id.*

Since seborrhea and seborrheic dermatitis are different disorders and involve different cells: the sebaceous glands (seborrhea) and the keratinocytes (seborrheic dermatitis), Dr. Leyden explains that seborrhea is not a subset of seborrheic dermatitis, nor is seborrheic dermatitis a subset of seborrhea. *Id.* at ¶ 7. As a result, not every seborrhea patient has seborrheic dermatitis, and vice versa. *Id.* at ¶ 8.

In view of the above, the Saint-Leger disclosure of a variation in seborrhea in its Example 6 is not a suggestion to treat the different condition of seborrheic dermatitis. The Saint-Leger patients are not disclosed as having seborrheic dermatitis, but rather having some degree of seborrhea. Even with respect to the disclosed condition of seborrhea, Saint-Leger does not identify which of the active agents in its composition would be responsible for the variations in the condition. Any conclusion now drawn that the compound of the present invention, used as the sole active ingredient, would be useful in the treatment of seborrheic dermatitis, can only be based on improper hindsight while also disregarding how a person skilled in the art would have viewed the differences between the two conditions as explained by Dr. Leyden.

In the Advisory Action, the Examiner cited three additional U.S. patents for the proposition that the same drug treatment will treat both seborrhea and seborrheic dermatitis, due to alleged common patho-etologies between the two conditions. As explained above, however, the treatment of one does not equate with the treatment of the other. Again, since seborrhea and seborrheic dermatitis are different disorders and

involve different cells: the sebaceous glands (seborrhea) and the keratinocytes (seborrheic dermatitis), seborrhea is not a subset of seborrheic dermatitis, nor is seborrheic dermatitis a subset of seborrhea. *Id.* at ¶ 7.

The first patent cited by the Examiner, U.S. Patent No. 4,172,149, appears to indicate at col. 1, lines 11-15, that seborrhea is one component of the pathology of seborrheic dermatitis. As explained by Dr. Leyden, that interpretation in the patent is simply wrong. Leyden Declaration at ¶ 9. Moreover, a dermatologist would not normally use an anti-seborrheic agent to treat seborrheic dermatitis. *Id.* at ¶ 11. This is especially true because dermatologists often see seborrheic dermatitis in patients who don't have seborrhea, and therefore know that seborrhea is not a subset nor the same as seborrheic dermatitis and seborrheic dermatitis is not a subset of seborrhea. *Id.* Put another way, a physician will not use a treatment for seborrhea in connection with a disorder, such as seborrheic dermatitis, which is known to be different in both cause and effect from seborrhea. *Id.*

The second patent cited by the Examiner, U.S. Patent No. 6,120,756, states at col. 6, lines 30-32, that seborrheic dermatitis "as used herein is defined as chronic inflammatory disease of the skin associated with excessive sebum production." Dr. Leyden explains that while this patent may so define this term for its own purposes, that does not reflect the understanding of the art. Leyden Declaration at ¶ 10 (citing Fitzpatrick's Dermatology in General Medicine). Seborrheic dermatitis is a chronic inflammatory disease of the keratinocytes but it is not associated with excessive sebum production. *Id.* Many, if not most, patients with seborrheic dermatitis do not have excessive sebum production. *Id.* In fact, there is no evidence that seborrheic dermatitis is associated with either increased or decreased sebum production. *Id.*

The last patent cited by the Examiner, U.S. Patent No. 6,099,870, issued on August 8, 2000, and claims U.S. priority only as far back as December 18, 1997. The present application has an effective U.S. filing date of September 16, 1997. The '870 patent disclosure therefore should not be prior art to the pending claims.

In view of all of the above, the pending rejection of the claims in view of Saint-Leger, whether taken alone or in combination with the newly-cited references, should not anticipate or render the claims obvious.

The Examiner additionally rejected claim 19 as having been obvious over Saint-Leger in view of U.S. Patent No. 5,132,107 to Lange. Even in combination with Lange, and in addition to the arguments with respect to Saint-Leger already presented above, there is no suggestion or teaching of the claimed invention. Lange teaches a "two phase" composition meaning, in effect, that there are two different compositions which are not compatible, are packaged separately, and must be applied sequentially. (See Col. 2, lines 5-12, Col. 6, lines 39-57). The compositions must be used in the particular order described in the patent. (Col. 2, lines 13-20). Therefore, Lange does not suggest applicants' invention of a single composition with only the recited antifungal agent as its active component.


Lastly, the applicants acknowledge that the Examiner maintained a provisional double patenting rejection over the claims of co-pending application no. 09/077,194. In the event that the '194 application issues as a patent, applicants will consider providing a terminal disclaimer if appropriate.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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